What is claimed is:

1. A method of therapeutically downmodulating an autoimmune response in a subject comprising administering an antigen binding portion of an anti-CD28 antibody that blocks signaling via CD28 to the subject such that an autoimmune response in the subject is downmodulated.

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2. The method of claim 1, wherein the antigen binding portion is an scFv molecule or an Fab fragment.

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- 3. The method of claim 1, wherein the antigen binding portion is humanized.
- 4. The method of claim 1, wherein the antigen binding portion is fully human.
- 15 5. A method of therapeutically downmodulating an autoimmune response in a subject comprising administering a small molecule that specifically blocks signaling via CD28 to the subject such that an autoimmune response in the subject is downmodulated.
- 6. The method of claim 1 or 5, wherein the autoimmune response is mediated by CD4+ 20 T cells.
 - 7. The method of claim 1 or 5, wherein the autoimmune response is mediated by CD8+ T cells.
- 25 8. The method of claim 1 or 5, wherein the autoimmune response is type I diabetes.
 - 9. A method of therapeutically downmodulating an ongoing autoimmune response in a subject comprising administering an antigen binding portion of an anti-CD28 antibody that blocks signaling via CD28 to the subject such that an ongoing autoimmune response in the subject is downmodulated.

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- The method of claim 9, wherein the antigen binding portion is a scFv molecule or an 10. Fab fragment.
- The method of claim 9, wherein the antigen-binding portion is humanized. 11.

The method of claim 9, wherein the antigen-binding portion is fully human. 12.

- A method of therapeutically downmodulating an ongoing autoimmune response in a 13. subject comprising administering a small molecule that specifically blocks signaling via CD28 to the subject such that an ongoing autoimmune response in the subject is downmodulated.
- 14. The method of claim 9 or 13, wherein the autoimmune response is mediated by CD4+ T cells.
- 15. The method of claim 9 or 13, wherein the autoimmune response is mediated by CD8+ T cells.
- 16. The method of claim 9 or 13, wherein the autoimmune response is type I diabetes.
- 17. A method of prophylactically downmodulating an autoimmune response in a subject comprising administering an antigen binding portion of an anti-CD28 antibody that blocks signaling via CD28 to the subject such that an autoimmune response in the subject is downmodulated or delayed in its onset.
- 18. The method of claim 17, wherein the antigen binding portion is a scFv molecule or an Fab fragment.
- The method of claim 17, wherein the antigen-binding portion is humanized. 19.
- 20. The method of claim 17, wherein the antigen-binding portion is fully human.

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- 21. A method of prophylactically downmodulating an autoimmune response in a subject comprising administering a small molecule that specifically blocks signaling via CD28 to the subject such that an autoimmune response in the subject is downmodulated or delayed in its onset.
- 22. The method of claim 17 or 21, wherein the autoimmune response is mediated by CD4+ T cells.
- 23. The method of claim 17 or 21, wherein the autoimmune response is mediated by CD8+ T cells.
- The method of claim 17 or 21, wherein the autoimmune response is type I diabetes. 24.

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